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SHOULD VITAMIN D BE GIVEN ONLY TO INFANTS?

VITAMIN D has been so successful in preventing rickets during i fancy that there has been little emphasis on continuing its use afi the second year.

But now a careful histologic study has been made which reve a startlingly high incidence of rickets in children 2 to 14 years ol Follis, Jackson, Eliot, and Park* report that postmortem examin tion of 230 children of this age group showed the total prevalen of rickets to be 46.5%.

Rachitic changes were present as late as the fourteenth year, an the incidence was higher among children dying from acute disea than in those dying of chronic disease.

The authors conclude, "We doubt if slight degrees of ricket such as we found in many of our children, interfere with healt and development, but our studies as a whole afford reason to pro long administration of vitamin D to the age limit of our study, th fourteenth year, and especially indicate the necessity to suspect an to take the necessary measures to guard against rickets in sic children."

*R. H. Follis, D. Jackson, M. M. Eliot, and E. A. Park: Prevalence of rickets in childr between two and fourteen years of age, Am. J. Dis. Child. 66:1-11, July 194

SPECIAL REPORT

BURNS

George William Ware, M.D.

It has been estimated that 6,000 persons die each year due to burns.[27] The economic and psychologic problems of the untold thousands who live and are scarred permanently can never be completely told. Our attack on burns must be twofold—prevention and treatment. Since over 80% of burns occur in the home, prevention should be directed here primarily. Public education should be undertaken. Campaigns similar to those formerly directed towards appendicitis and the present campaign against cancer should be planned. The treatment has changed greatly, important strides having been made in the past eight years. An attempt will be made to enumerate some of these changes and to give a general outline of the treatment as used at Children's Hospital.

Classification: Burns are classified as first, second or third degree. A first degree burn is one which causes redness or erythema of the skin. An example of a first degree burn is the ordinary sunburn. A second degree burn is one in which there is blister formation with some destruction of the outer layers of the skin. An example of this type is the minor injury sustained by the housewife in cooking. A third degree burn causes destruction of all the layers of the skin and may involve underlying subcutaneous tissue and muscle. It is of course the most severe type and is exemplified by the injury due to burning of the victim's clothing.

Extent:[21] The area involved is of great import. It should be estimated and recorded at the first examination of the burn. It has been estimated that burns of the head constitute an involvement of 6% of body area. The trunk constitutes 38% of the body; the upper extremities comprise 18% and the lower extremities make up 38%.

Pathology: The depth and extent of body surface involved may be misleading in an infant or child. It must be remembered that subcutaneous tissue increases with age. A burn of a certain depth causing a second degree burn in an adult would cause a third degree injury involving muscle in an infant. Furthermore, an apparently restricted burn in an infant may, in fact, represent involvement of a seriously large fraction of the body surface.

1. *Edema:* This finding is most pronounced in second and third degree burns. However, there is an important difference between the two types. In second degree burns the outpouring is often most after the first 48 hours. This is due to the fact that the eschar in third degree burn acts

like a pressure dressing in the early stage. With time this eschar softens and begins to slough. With this slough external edema becomes evident. The internal edema, namely fluid loss into the tissues, is present as in second degree burns during the first forty-eight hours.

The amount of fluid loss in this edema is considerable. The loss has been shown by Blalock to be sufficient to cause shock.[2] This evidence forms the rationale of pressure dressing.[2,3]

The content of the fluid is important. Its composition is similar to that of plasma. It is not a mere watery exudate. The albumin content of the fluid is 80% that of plasma, the globulin concentration is 55–75% that of plasma.

2. *Lungs:*[11–14] The lesions seen here will vary with the duration of the burn. They include the inhalation of noxious gases at the time of the burn, pulmonary edema due to overstrenuous fluid replacement and bronchopneumonia during the hospital stay. The latter two will be considered first.

Pulmonary edema due to fluids can be avoided by proper calculations of needs and the rate of administration. Bronchopneumonia is not due to the burn per se but rather to the invalid state following the burn. Its pathological picture does not vary from the disease as seen in the aged who are confined to bed for long periods of time. Its prevention in the burn patient is the same as in the aged invalid.

The major respiratory lesion in the acute phase is a laryngo-tracheo-bronchitis similar to the disease seen in infants. It is of varying degrees of intensity and is essentially a fibrinous pseudo-membrane of the respiratory tree with a thick mucoid and sanguinous exudate. Its severity does not bear any constant relation to the severity of the surface burn. Aspiration of the sloughed portions of this membrane may lead to atelectasis. Other respiratory lesions are hemorrhage or infarcts due to vascular thrombosis.

Fluid therapy in patients with laryngo-tracheo-bronchial lesions forms a difficult problem because of the fear of causing pulmonary edema. However, in treating patients of the Coconut Grove fire, it was found that in the presence of shock these patients do better with the usual fluid replacement therapy.[12] They received the same fluids as the patient without respiratory damage except that somewhat less saline was given. These patients were more frequently and carefully examined for the possible development of pulmonary edema.

It was also found that oxygen was essential in treating these people. Many of these victims have dyspnea and varying degrees of anoxia. They were very difficult to manage and in some cases developed an acute mania. This state did not respond to sedatives but was cured dramatically by oxygen.

Tracheotomy was of little or no value in the treatment of these patients.

3. *Liver:* Since the abandonment of tannic acid in the treatment of burns, the importance of the liver pathology has decreased. It is now believed that there is an impairment of liver function of a transitory nature during the period of toxemia and that it plays a minor role in the overall picture.

4. *Stomach:* Curling's ulcer of the stomach and duodenum is still occasionally seen. It is to be suspected with hematemesis or symptoms of an acute surgical abdomen due to perforation. It is now believed that its development is due to hemoconcentration and can be prevented with adequate fluid therapy.[15]

5. *Kidney:*[17, 20, 21, 29, 38] Here the most important pathological findings are in the tubules. Casts appear and are due to intravascular hemolysis. These casts give a positive reaction for hemoglobin and are undistinguishable from those seen in the kidney following a transfusion reaction. The microscopic changes in the tubules vary from cloudy swelling to a true necrosis. In cases that survive over 5 days tubular regeneration has been shown to occur. The pathological picture in general is similar to that seen in transfusion reaction, crush syndrome or prolonged surgical shock.

The development of oliguria and anuria has always been a serious problem and has not been completely solved as yet. Several possible causes include inadequate fluid replacement and shock. The presence of shock per se will reduce the renal output. The degree of oliguria, however, is not directly proportional to the degree of shock. Reduction of cardiac ouput by 50% reduces renal blood flow by 90 to 95%.

Oliguria and anuria were once attributed to intravascular hemolysis and precipitation of hemoglobin in the tubules in the presence of an acid urine. However, fatal anuria may develop in the presence of an alkaline urine. Also mere injection of hemoglobin in experimental animals causes variable renal damage but never serious enough to cause anuria. This was consistently true whether or not the urine was acid. However, if shock sufficient to produce renal ischemia is present, the injection of hemoglobin will then produce anuria. Hence it is now believed that precipitation of hemoglobin in the tubules may aggravate oliguria but does not per se cause the anuria.

Trueta believes that the oliguria is due to reduced glomerular circulation and resultant low filtrate formation combined with tubular damage resulting in increased unselective reabsorption.[38] The reason for this reduced glomerular circulation is still unknown. The effect is mediated through the splanchnic nerves inasmuch as severance of these nerves prevents such a change in the renal circulation.

6. *Anemia:* This is a constant finding and a considerable handicap.

Next to infection, it is the most distressing feature once the initial crisis is past. The only way that it is to be overcome is by early strenuous treatment and awareness of its insidious development in the stage of repair.

It should be realized that an anemia exists shortly after the burn. The belief that an anemia develops only after two to four days in the hospital is false. Anemia, gauged by laboratory reports, develops at that time because by then replacement therapy and the redistribution of body fluids make it apparent. Waiting until a laboratory anemia develops may cost the life of the patient and certainly greatly prolong his hospital stay.

The causes of the anemia are as follows:[21]

a. Early intravascular hemolysis due to the heat of the substance causing the burn.

b. Loss of cells through the open granulating wound.

c. Infection.

d. Depressed bone marrow function. This is shown by low reticulocyte counts and has also been demonstrated by studies using radioactive iron.

e. Finally a burn is a general metabolic disorder affecting the gastrointestinal tract and liver.

Treatment: The treatment other than first aid should be directed by an experienced and interested surgeon or according to specific principle outlined by him and under his guidance. The treatment as given at Children's Hospital has been conceived by the Chief of the plastic service, and has been carried out under his supervision.

It is felt at Children's Hospital that the person in charge should be able to care completely for the patient. There should be no confusion or division of authority. The person in charge must be able to form a reliable opinion as to the degree and extent of the burn, dress the patient and estimate his metabolic needs. He must know when to change dressings, how to treat the various types of infection should they arise and finally he must know how and when to graft.

There must be a basic plan of treatment. Fluids must be ordered in consideration of the basic metabolism of the patient and his extra needs due to his burns. This plan may be varied according to changing needs as shown by laboratory data. However, one cannot await laboratory reports before instituting treatment. Time in units of hours is extremely important. Foresight is essential in the successful treatment. One can never allow the treatment to lag. If there is any doubt one should always overtreat. It is easier to cancel an order for parenteral fluids due to a favorable laboratory report than it is to give additional fluids to make up for an earlier miscalculation. This is extremely important in the treatment of infants and children. In this group the onset of shock is often without warning and is frequently irreversible. For this reason the care of burns in children must be assiduous.

1. *Emergency Room:* Under ideal conditions there should be a room set aside for the first aid treatment of burns. The child should be stripped of all clothing and wrapped in sterile sheets. This is done by masked internes and nurses. No attempt at cleansing is performed at this time. The temperature, pulse and blood pressure are recorded. An evaluation of the depth and extent of the burn is made. Sedation is freely given if shock is not in evidence. If shock is present, a hematocrit is first determined, then plasma therapy and oxygen are started.

2. *Operating Room:* After these early procedures have been swiftly accomplished the patient is taken to the operating room. Anesthesia consists in the use of morphine or for younger patients barbiturates. Cultures are taken from all areas of the burn and are carefully labeled as to the site. The burned area is cleansed with green soap and water. There is no extensive scrubbing. Any gross contamination is removed. The areas are then rinsed with sterile saline solution. Rayon dressings are then applied next to the skin[35] over which heavy pressure dressings are used.[23]

3. *Ward:* While these measures were being performed in the operating room, the ward nursing staff was alerted concerning the admission. When the patient returns to the ward, hematocrit tube, plasma and intravenous tubing are ready by the bedside. Withdrawal of hematocrit sample and the start of the infusion take precedence over the other ward tasks.

Various schedules have been advised for plasma dosage: (a) 100 cc. for every point which the hematocrit exceeds 45,[18–21] (b) 50 cc. for every per cent burn of body area,[18–21] (c) for small children, 5 cc. of plasma per pound of body weight for the first intravenous dosage.[28]

If the burn is 10% of body area or over, blood is given the day of admission or the following day depending on the rapidity with which hemoconcentration is conquered.

Normal saline in glucose solution (5%) is used in equal amounts to plasma and is given intramuscularly or subcutaneously. Berman has recommended subcutaneous injection of saline (in place of plasma) into the burned area to increase tissue pressure and thus combat exudation of plasma.[3, 4]

Since the greatest change in hematocrit occurs in the first six hours, the value is checked every one to three hours depending on the severity of the burn. If the patient is a small child and blood samples are difficult to obtain, red blood counts and hemoglobin determinations may be substituted. Here again experience and knowledge of the severity of the burn will modify the interpretation of these reports.

Blood pressure, pulse, temperature, and respirations are charted every hour for 12 to 24 hours.

A careful itemized intake and output record is kept. If any doubt

exists as to the urinary output in a small child, a catheter is immediately placed in the bladder. Urinalyses for specific gravity and acetone are done at least twice a day for the first three days. Additional urinalyses for albumin, microscopic examination and occasionally for the presence of hemoglobin are done daily. The urinary output at all times is kept at the same level as that of a normal child. Great reliance is placed on the urinary output and specific gravity of the urine as guides to the status of the patient.

The nutrition of the patient is cared for by parenteral therapy in the first few days. If the patient is able and willing to eat, the outlook is better. However, we do not wait to see if this will be the case. To maintain nutritional requirements a venesection may be necessary or a special formula may be administered by gastric drip.[33]

Penicillin is used routinely. Other drugs are used as indicated below.

Following this initial therapy, care of the patient is continued with a careful plan to prevent anemia and low protein level. The temperature is watched for signs of infection.

In ten to fourteen days the patient is redressed. Cultures are repeated at this time. A second evaluation of the burned area is made. If grafts are deemed necessary they are done on the day of the first dressing or shortly thereafter. In no case should grafting be prolonged beyond 21 days after admission. If the patient is still toxic or anemic at this time, it is an indication that early treatment was inadequate. The best results are obtained with early grafting.[9] In some instances, e.g. localized third degree burns, grafting may be done on the day of admission to the hospital. Early and repeated grafting will reduce greatly the hospital stay. However, vigorous early care will insure that the patient will be ready for grafting in 10–14 days following injury. Pressure dressings are applied and the graft is inspected in five days. This procedure is repeated as often as is necessary.

Complications: 1. Shock early in the post-burn period.

2. *Anuria.* The development of anuria in children is a bad prognostic sign. First it should be determined whether it is due to shock or inadequate fluid therapy. If so it is rapidly treated. If not due to these factors, the mechanism suggested by Trueta is kept in mind, namely decreased glomerular circulation. To combat this, isotonic sodium sulfate in amounts from one fifth to one third of total daily fluids is used intravenously.[26, 32, 33, 37] Since this effect is mediated through the splanchnic nerves, local block of these nerves has been used in our hospital.[1, 38]

3. *Eschar of third degree burn.* One of the greatest barriers to complete healing of third degree burns has been the formation of a thick hard eschar. This rigid slough has permitted infection to persist, allowed the continued

loss of fluids and prevented grafting which would close the open wound. Recognition of these factors has led to the use of many substances to combat this slough.[5, 7, 16] The most effective preparation seems to be pyruvic acid as originally used by Cannon and Harvey[5, 6] and recommended by others.[36] In the limited experience of Children's Hospital it has proved to be of great value.[39] In our cases only two applications done at forty-eight hour intervals have been required. With such a routine we have observed complete or nearly complete separation of the slough in this short time. Wet dressings were then used for another forty-eight hours and then grafting was performed.

4. *Infection.*[2, 4] Penicillin is used routinely and is started at the time of entry into the hospital. Cultures are taken at the time of entry and at each subsequent dressing. According to the growth obtained from these cultures, penicillin is continued, augmented or replaced by various drugs.

a. *Organisms encountered:* 1. *Bacillus subtilis.* This is considered separately for it is most commonly seen. It is usually easily handled by two per cent acetic acid soaks[34] or by tyrothricin soaks.

2. *Staphylococcus.* This may be treated adequately in the early stages by penicillin. Resistance, however, quickly develops and if persistent cultures are obtained the sulfonamides should be used.

3. *Streptococcus* (alpha and beta). Here sulfonamides are added to the penicillin therapy. If treated by the latter alone, the infection may even spread.

4. *Gram negative bacilli.* These are most commonly seen with wounds of the buttocks and thighs. They are difficult to eradicate. Frequently they do not make their appearance on the culture plate until the second week. Penicillin is useless against them, in fact it is inhibited by them. To eradicate their presence streptomycin should be given parenterally, sulfathalidine or streptomycin should be given orally and streptomycin or tyrothricin used locally in the form of soaks.

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NEWBORN INFANTS OF DIABETIC MOTHERS

Case Report No. 139

Robert O. Warthen, M.D.

B. T., a white male infant, was born of a diabetic mother after thirty-eight weeks gestation. During the last two months of the pregnancy the mother experienced a mild toxemia with edema of the lower extremities and minimal albuminuria. She had been under treatment for diabetes mellitus for over fourteen years and was well controlled with insulin (protamine zinc and crystalline) prior to, at the time of, and following delivery of the infant by Caesarean section. There had been no previous stillbirths or abortions.

The infant weighed 8 pounds 6 ounces at birth, was 20 inches long and exhibited pronounced generalized edema. Extreme cyanosis and dyspnea with periods of apnea occurred during the first 24 hours of life necessitating the use of an incubator. On the second and third days of life his respirations improved greatly and cyanosis was not noted as long as continuous oxygen was employed. Disappearance of the generalized edema and a weight loss of 22 ounces had occurred by the fourth day of life. Physiological jaundice, as confirmed by successive blood counts, appeared on the fourth day and gradually subsided. The inferior edge of the spleen was palpable at that time. He was transferred to a bassinet and oxygen was discontinued on the fifth day. A physical examination on that day disclosed no abnormalities.

The blood sugar at birth was 40 mgm. per cent, at eight hours of age 66 mgm. per cent, at 24 hours 40 mgm. per cent and at 30 hours 72 mgm. per cent. Twenty-five cubic centimeters of 10% glucose was given intravenously at 4 hours of age as a prophylactic measure.

An unexplainable fleeting period of apnea and cyanosis responding to oxygen occurred on the eighth day of life. Immediately after this episode the infant appeared entirely normal and a roentgenogram of the chest disclosed no abnormalities.

With the exception of the intravenous glucose given at four hours of life, no oral or parenteral fluids were employed for the first 48 hours in an attempt to dehydrate the edematous infant. From 48 to 72 hours 5% glucose in distilled water was offered orally and at 72 hours of age breast feeding was instituted.

The infant was afebrile throughout the twelve days of hospitalization and when discharged he weighed 7 pounds 2 ounces. At that time complete physical and neurological examinations revealed no abnormalities.

DISCUSSION

For many years newborn infants of diabetic mothers have been treated initially with parenteral and oral glucose because of the theory maintaining that a transient overactivity of the infant's hyperplastic islets of Langerhans results in a temporary hypoglycemia of the newborn. It is now well known that the low blood sugars previously believed to be in a hypoglycemic stage are actually normal for newborns. Normal newborn blood sugars usually range from 40 to 60 mgms. per cent with a low normal of 35 mgm. per cent (during the first day of life). The importance of hyperplasia of the isles of Langerhans in infants of diabetic mothers has also probably been overrated, for of 17 such autopsided infants[2] only five exhibited hyperplastic islets. In a study of 125 infants of diabetic mothers, Sisson and White[1,2] recorded newborn blood sugars ranging from 20 to 250 mgm. per cent with one exception. That was the case of an infant with a blood sugar of 9 mgm. per cent whose mother was in a state of hypoglycemia (insulin shock) during the delivery; the infant responded readily to glucose. White[2] also found that these infants had blood sugars transiently higher than levels encountered in normal newborns. In these infants an unexplainable fall in the blood sugar may occur during the first four hours of life (perhaps due to insulin received from the mother) followed by a spontaneous rise by the eighth hour of life. Inasmuch as the initial blood sugars in these infants are higher than normal, this early fall is usually of no consequence. Moderately uncontrolled diabetes during delivery, i.e. maternal acidosis and minimal insulin shock, has not been proved to be harmful to the infant.[2, 3] It is also quite comforting to know that none of the infants of diabetic mothers have been born with clinical diabetes.

Infants born of diabetic mothers usually exhibit an overall picture of post-maturity. The majority are longer and weigh more than average infants born after comparable gestation periods. The weight increase is due to the pronounced generalized edema, increase in body fat and splanchnomegaly (most striking in the liver, spleen and heart). These infants experience a more marked weight loss than average infants during the first three days of life because of the excessive loss of edema fluid shortly after birth. The 72 hour weight loss in a series of 125 infants reported by White[2] averaged 10.5 ounces; some infants losing up to 25 ounces. Significant numbers of abnormal infants of diabetic mothers are usually encountered. These abnormal newborns are frequently characterized clinically by respiratory distress, cyanosis and apnea. Pulmonary atelectasis, fibrillary twitchings, rapidly developing jaundice and unstable temperatures are prominent findings. The respiratory difficulty has been attributed to

cerebral edema, pulmonary atelectasis, aspirated amniotic fluid and aspirated stomach contents. Congenital defects and prematurity occur with a greater frequency in infants of diabetic mothers.

The mortality rate of these infants is significantly higher than normal, White[2] reporting a rate of 12 per cent in 125 cases. Over 70 per cent of the deaths were accounted for by macerated stillbirths and pulmonary atelectasis, whereas the remainder were due to subtentorial hemorrhages, hemorrhagic disease of the newborn, skull defect and erythroblastosis foetalis. Fetal fatalities are usually directly related to poor control of maternal diabetes, congenital defects of the infant, pronounced maternal vascular disease as the result of diabetes, and maternal hormonal imbalance.[4] Maternal hormonal imbalance probably accounts for many of the accidents characteristic of a diabetic pregnancy, such as pre-eclamptic toxemia, prematurity and fetal death. These accidents appear to be related to an abnormal increase in chorionic gonadotropin excretion and a decrease in pregnandiol (progesterone and estrogen) excretion. White[2, 4] has shown that this imbalance may be corrected by injection of substitutional therapy of estrogen and progesterone, thus alleviating the accidents so frequently encountered in these pregnancies.

The management of these infants is twofold; antenatal and postnatal.[4] Antenatal therapy involves the proper management and control of maternal diabetes (insulin, diet and exercise regulation), strict antepartum care, correction of any existing hormonal imbalances, and delivery of the infant (preferably at or before 38 weeks of gestation). Post-natal management as outlined by White[4] and as practiced by her group in Boston is as follows: Immediately after delivery the infant is inverted for about five minutes, thereby accomplishing postural drainage of the air passages. Following this the upper air passages are suctioned and the stomach is aspirated of all contents. The newborn is then placed in an incubator for at least three days in order to maintain adequate regulation of the body temperature and to insure a continuous flow of oxygen at six liters per minute. The upper air passages are suctioned every two hours for the first 12 hours of life and the stomach is aspirated every three hours for the same period of time. The infant is turned often and stimulated to cry frequently. No oral or parenteral fluids are administered for the first 48 hours in order to alleviate the generalized edema. A nursing routine is instituted after this initial period of dehydration.

The infant may be born in hypoglycemic shock if maternal hyperinsulinism exists at the time of delivery. It is therefore advisable to obtain infant blood sugar levels in selected cases at birth, at four and at eight hours of age. If any of these readings is below 35 mg. per cent, 50 cc. of 5 per cent glucose in distilled water should be administered parenterally.

Mortality and morbidity rates of infants of diabetic mothers have been significantly reduced under the therapy regime outlined above. These reductions have been largely attributed to a lessening of the respiratory difficulties that heretofore have been the primary problems of these infants.[4] Also of great importance are the improved methods of treating maternal diabetes and of controlling maternal hormonal imbalance during pregnancy.

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STREPTOCOCCUS MENINGITIS IN THE NEWBORN

With Report of Cases in Identical Twins

Case Report No. 149

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Meningitis of the newborn (three weeks of age or less) is uncommon and characterized by an atypical clinical picture. The streptococcus as an etiologic agent in newborn meningitis is rare and this discussion and report represents what is apparently the first reported in identical twins with the recovery of the organism from a clinically asymptomatic mother.

LITERATURE REVIEW

Smith[1] in 1928 collected cases of newborn meningitis from the literature of which six, those of Holt[2] and one of Smith's cases, were due to the streptococcus. Lindsay et al.[3] in 1932 discussed the cases of Gueniot.[4] Fothergill and Sweet[5] reported nine cases in the newborn due to streptococcus. Gibel and Litvak[6] in their careful review of the literature of hemolytic streptococcus meningitis in infants under three months covered a period from 1895 to 1942 and listed 29 cases including those of Holt, Smith and Fothergill, where the etiology was definitely known and the age under three weeks. Hurst and Astrowe[7] reported a case in 1941 in a premature infant whose mother underwent an emergency hemorrhoidectomy 30 hours before delivery. Other reports in the literature have been made of meningitis under three months but without definite mention of the exact age or causative agent; therefore the total number of cases listed above probably does not represent all. With the advent of chemotherapy and penicillin the mortality in this disease has been reduced so markedly that often it is no longer deemed necessary to report such cases.

ETIOLOGY

The etiology is more often obscure. The infection may occur by direct extension from the mouth, umbilicus, nasopharynx, gastro-intestinal tract, skin, mother's birth canal, a spina bifida or an incidental lesion through which the organism is introduced during delivery. By hematogenous or lymphatic extension the meninges may be involved from the orbit, ears, etc. A definite history of a meningitis in the mother, an upper respiratory infection or birth injury may be the source. When these conditions are

not present theories are substituted. Many believe that intrauterine meningitis is not infrequent. Premature respiration with aspiration may be the cause and the disease could be milk borne after birth.

CLINICAL SIGNS AND SYMPTOMS

Clinically, in the newborn, the classic signs and symptoms are conspicuously absent. Fever, convulsions, irritability and crying are most frequent. Nystagmus, excessive response to external stimuli, muscle spasm, cyanosis and dyspnea occur. An abnormal fontanel is not present in most instances. Due to the incompletely developed nervous system at this age the usual signs of meningitis are rarely present. Vomiting and diarrhea may occur.

DIAGNOSIS

Because of the similarity to other conditions at this age the diagnosis is often difficult. The onset is insidious and the clinical picture develops slowly. Thus with the picture indefinite, the disease is usually fully developed before the diagnosis is made. The disease often escapes recognition because of the confused picture for 24 to 48 hours while the effects of supposed birth trauma are allowed to subside.

PROGNOSIS AND TREATMENT

The prognosis is poor even with the specific chemotherapeutic agents and penicillin. This is due in most part to the advanced stage of the disease before the diagnosis is realized. Vigorous supportive therapy with fluids, blood, etc., is necessary as would be expected with a newborn with a severe infection.

CASE REPORT

The mother of the patients, a colored 22 year old primipara, was admitted to the obstetrical department of Garfield Memorial Hospital in June 1942. The pregnancy had been normal and the physical examination was normal except for the evidences of impending birth. Temperature, pulse, respiration, routine blood examination, urinalysis and Kahn were negative. No vaginal examinations were performed. With the usual preoperative medications and under ether anesthesia after 36 hours of labor identical twin girl infants were delivered.

Twin #1 was in the left occiput position and delivered with the aid of low forceps. The infant's weight was 2,354 grams, length 58.3 cm. The cry was immediate and the child was considered normal. It was placed on breast milk and evaporated milk feeding and seemed to thrive until the eighth hospital day. Constant crying ensued and the temperature rose to

102.4 degrees F. This behavior, characterized by restlessness, crying, anorexia continued on the ninth day with the temperature remaining at 102 degrees F. Subcutaneous and intravenous fluids were given. On the 10th day with the temperature at 102.4 degrees F., a spinal tap was performed which showed a cloudy, xanthochromic fluid with 800 cells per cu. mm., of which 100 per cent were lymphocytes. Bacteria were not found on smear. Culture revealed a hemolytic streptococcus. The child was transferred to the Children's Hospital on the tenth day and placed on sulfadiazine, parenteral fluids and an evaporated milk formula. The infant exhibited few clinical symptoms except for irritability, intermittent refusal to eat and a temperature elevation ranging about 100 to 102 degrees F. The latter returned to normal on the fourth Children's Hospital day and except for a short spike on the fifth and sixth day remained at a normal base level throughout the entire hospital stay. Laboratory work showed that the patient maintained a leucocytosis throughout most of the hospital period ranging from 10,000 to 20,000. Spinal fluid obtained on the second hospital day showed 165 cells per cu. mm. with 76 per cent polymorphonuclears and 24 per cent lymphocytes. Culture of ventricular fluid and cisternal fluid taken the same day showed gram positive cocci in chains. Small blood transfusions were given in addition to general supportive measures and the sulfadiazine was discontinued on the fourteenth hospital day. The infant continued to gain weight and improve and was discharged after 24 days as recovered.

Twin #2 was in the right sacrum anterior position and a version breech delivery was done. The weight was 2,752 grams, length 58.2 cm. The child cried immediately and was considered normal. The hospital course was normal and the infant thrived on a formula of breast milk plus evaporated milk. It was discharged after nine days. Three days later the infant's father noticed that the child was very hot, cried continually and refused to nurse. The following day it appeared to have difficulty breathing and was cyanotic. It became stiff when touched. The infant was admitted to the Children's Hospital where physical examination showed an acutely ill infant appearing slightly jaundiced. The skin was hot and dry. The anterior fontanelle measured 2.5 cm. across and was bulging but not tense. The eyes showed oscillatory movements and a lateral nystagmus. The remainder of the examination was negative, there were no injuries, and the umbilical area showed normal healing. The temperature was 102.2 degrees F. and rose in a few hours to 103 degrees F. First attempts at lumbar puncture were unsuccessful and bloody fluid was obtained. A repeat procedure 2½ hours later showed cloudy, xanthochromic fluid under increased pressure. Culture of this fluid showed a hemolytic streptococcus. The infant was treated with sulfadiazine, intravenous and subcutaneous

fluids and oxygen. Ten hours after admission the child had two generalized convulsions lasting about one minute. Cyanosis became more marked with shallow, labored respirations. Respiration ceased 12 hours after admission, 13 days after birth. Autopsy revealed a few disseminated hemorrhage suffusions on both arms and on the right side of the head. The fontanelles did not bulge and were open. Both hemispheres and the base of the brain were covered with a small amount of mucoid, greenish-yellow pus. The gyri appeared flattened. The meningeal vessels were markedly congested and some veins over both parietal lobes and over the right half of the base of the brain were dilated and thrombosed. The right lateral and occipital sinuses were filled by clots suggesting thrombosis. Smears and culture from the meninges showed a gram positive cocci in chains. The lungs were intensely congested throughout, with scattered areas rather firm and non crepitant. Cultures from the lung showed a streptococcus exhibiting slight hemolysis. The spleen was also congested and culture from the organ showed a similar growth of organisms. The remainder of the organs were normal.

The postpartum condition of the mother was normal. At no time did she exhibit any clinical manifestations of an illness. A spinal puncture was performed and the fluid showed similar streptococci to that found in the fluid of the twins. There was no chemical or cellular change in the fluid. The possibility of a contaminant must be considered but inasmuch as the organism was recovered in both infants at this age period and at the same time as the mother, the results appear correct.

DISCUSSION

The cases are noteworthy inasmuch as one bacteriologic etiology was proven in the three patients. The subclinical case of meningitis in the mother can be thought of along with many similar illnesses that are never diagnosed or treated when the patient does not reach a physician. Rantz[6] entertained the idea that in certain cases of streptococcus meningitis due to an unusual group of organisms, the patient may have a mild clinical course. We have seen cases of spontaneous recovery without drugs or recovery before chemotherapy was instituted.

SUMMARY

1. A brief review of the literature concerning meningitis in the newborn is given.

2. The report of streptococcus meningitis in newborn identical twins is made. One of the patients recovered. The same organism was cultured from the spinal fluid of the mother who remained asymptomatic.

3. These are believed to be the first reported cases in the literature of meningitis in identical newborn twins.

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TUBERCULOUS MESENTERIC ADENITIS

Case Report No. 141

Edward Curran, M.D. 48–4515

J. B., an eight year old Mexican boy, was admitted to the Children's Hospital on the evening of April 17, 1948 complaining of abdominal pain. He had been well until the morning of admission when he complained of vague, paraumbilical pain which subsided after several hours. Five hours later the pain recurred and steadily became more severe, being confined to the lower abdomen, particularly in the right lower quadrant. Shortly prior to admission, he became nauseated but did not vomit. About 14 hours prior to admission he had a normal bowel movement. Prior to admission he had two leucocyte counts reported as 19,000 and 24,000 respectively. No history of previous similar episodes was elicited.

The temperature upon admission was 101°, pulse 90 and respirations 24. The patient was well developed, well nourished and did not appear acutely ill. He lay quitely in bed, and could shift position without difficulty. Noteworthy findings were confined to the abdomen which was moderately rigid in both lower quadrants with diffuse lower abdominal tenderness, more evident in the right lower quadrant. There was no distension, and normal peristalsis was audible. No abdominal masses or organs were felt. Rebound tenderness was consistently encountered in the right lower quadrant. Rectal examination was non-informative.

A hemogram on admission revealed a leucocytosis of 13,900 of which 52 per cent were segmented, 20 per cent bands, 3 per cent metamyelocytes, 23 per cent lymphocytes and 2 per cent monocytes.

A provisional diagnosis of acute appendicitis was made and after routine preparation the abdomen was entered through a McBurney incision. A sero-purulent exudate was encountered on entering the peritoneal cavity. A moderately inflamed appendix was found which was removed, and its stump carbolized and inverted. Since it was felt that the condition of the appendix was not an adequate explanation for the presence of the peritoneal exudate, further exploration was carried out. In the mesentery of the ileocecal region at a point 8 cm. from the ileocecal junction a 5 cm. mass was found. After extension of the original McBurney incision, this purplish black mass situated within the mesentery was removed with some difficulty because of its intimate relation with the ileocecal artery. Other regional mesenteric nodes were palpably though not markedly enlarged.

On pathologic examination of the mass a diagnosis of hyperplastic tuberculous lymphadenitis was made. No growth was obtained from the culture

of the pus taken at the time of laparotomy. No tubercle bacilli were demonstrated in the specimen.

The postoperative course was uneventful. A tuberculin test was reported positive on April 21, 1948. On April 22, 1948, a chest film was reported as showing some perihilar fibrosis and calcification that had the appearance of a healed primary complex.

The patient was discharged on the eighth hospital day.

DISCUSSION

Juan I. Bustamente, M.D. (father of the child): It has been the custom in Mexico for at least 300 years to bring all milk to a boil and to allow it to cool before serving. My own family has been particularly strict in this respect. It is doubtful if my mother ever served milk which had not been boiled. My own household was also very strict in this respect.

Mexican herds are not tested for tuberculosis and milk is not pasteurized. The custom of boiling milk, if adhered to, is adequate protection. I believe that this is a tuberculous infection of bovine origin. However, we must yet isolate and study the organism to prove it.

If proved to be tuberculous, this infection was undoubtedly acquired in this country. In Mexico, the boy never drank milk that had not first been boiled. In this country his milk is usually pasteurized.

Byron K. Olson, M.D.: If the organism is recovered from cultures from the peritoneal fluid or the specimen, they could be differentiated by animal inoculation. The bovine form is very virulent to the Belgium hare. The human form is equally virulent to the guinea pig. However, the bovine form produces a minimal infection in the guinea pig whereas the human form produces a very minimal infection in the hare.

It might be well to remember that while pasteurization of milk and the testing of herds give a high degree of protection if correctly executed, neither is perfect. Both are necessary adjuncts to one another. The degree of protection varies directly with the care with which testing and pasteurization is carried out.

Robert Coffey, M.D.: In my experience the occurrence of non-specific mesenteric adenitis involving the ileocecal glands is one of the most common findings encountered in pediatric surgery. However, the occurrence of tuberculous mesenteric adenitis is a rarity and this represents the first case in my experience.

Tuberculosis of the gastro-intestinal tract generally is of infrequent occurrence today, except in those individuals who have an active pulmonary lesion. It might be presumed, I believe, that this represents a bovine tubercle bacillus infection, and I have been told by the late Dr. Will Mayo that prior to routine pasteurization of milk, involvement of the cervical

lymph glands by the bovine tubercle bacillus was a frequently encountered condition, and that similar involvement of the mesenteric nodes did occur, though less frequently. At the time of operation the firmness of the mass suggested that it might be a lymphoma or some other neoplastic lesion. However, since no intrinsic lesion of the bowel was found the operative procedure was limited to local excision of the gland.

CLINICO-PATHOLOGICAL CONFERENCE

Directed by: E. Clarence Rice, M.D.
Assisted by: Adrian Recinos, Jr., M.D.
Harold W. Bischoff, M.D.
By Invitation: Claude Frazier, M.D.

drian Recinos, Jr., M.D.

A two and one half year old Chinese female was referred from the Episcopal Hospital where she had been observed for inflamed and bulging eyes.

For five or six months the child had been noticed to have bulging eyes and a "lump on the throat." She had been well otherwise and her nutrition had not been altered. There was no history of excessive perspiration, tremors, weakness, or "nervousness." There were no gastro-intestinal, genito-urinary or neurological symptoms.

The child was delivered uneventfully at term and weighed seven and one half pounds. Her nutrition and development were normal. There had been no contagious diseases, immunizations, accidents or operations. She had been seen on various occasions in the Dispensary for minor complaints.

The family history was not contributory. The parents were natives of Canton, China and were not familar with any illnesses of their relatives.

Examination on admission revealed a well nourished and well developed oriental child appearing of the stated age. She was extremely irritable and acutely but not critically ill. The temperature was 101 degrees, pulse 150, and respirations 30 per minute. There was a moderate bilateral exophthalmos and the palpebral fissures were narrowed. The pupils reacted to light. The pharynx and tonsils were inflamed. A mass thought to be the thyroid could be felt in the anterior aspect of the neck, particularly on the right side. The heart was not thought to be enlarged. The apex beat was forceful and rapid. There were no thrills or murmurs. The lungs were clear, no organs or masses could be felt in the abdomen, and there were no abnormalities of the extremities. The deep reflexes were normal or slightly hyperactive.

A blood count on admission disclosed a hemoglobin of 11 gm. per cent, leucocytes 18,000 with 71 per cent neutrophiles and 29 per cent lymphocytes. Urinalysis was normal except for a two plus acetone and positive test for diacetic acid.

X-ray examination of the chest revealed the heart and lungs to be normal. The trachea was in the midline and there was a large supracardiac shadow extending from the apex to the third interspace anteriorly. An enlarged thymus or a widened superior vena cava were suggested to explain this shadow.

Twelve hours after admission the child became semistuporous and appeared critically ill. The temperature rose to 104° F. and the heart rate to approximately 200. The extremities were now flaccid and the reflexes absent. The blood sugar at this time was 40 mgm. per cent. The spinal fluid was normal in cellular and chemical content.

The child received symptomatic treatment only. She died 22 hours after admission.

DISCUSSION

Claude A. Frazier, M.D.: Let us first consider the history. The chief complaint was "inflamed and bulging eyes." The chief causes of inflamed eyes are infection, irritation, obstruction to the nasolacrimal ducts and protrusion of the eyeballs. There are a host of causes of exophthalmus. In a newborn we would think of hemorrhage in the middle fossa. Tumors of the orbit, such as sarcomas, osteomas, dermoid cysts, retinoblastomas, and metastatic neuroblastomas are responsible for *unilateral* exophthalmus. Rare causes of bulging eyes which seem unlikely in this case are Schüller-Christian disease, which was ruled out by the absence of typical symptoms, hepatosplenomegaly, and x-ray findings. Angioneurotic edema, scurvy, pertussis, epilepsy and thrombosis of the cavernous sinus were likewise ruled out by the history. Paget's disease and oxycephaly may cause exophthalmus but this child's head was presumably of normal size and shape. Syphilis of the orbit is a more common cause in the adult. We have no report of a serological test for syphilis and this patient is very young. The most common cause of bulging eyes in the adult and in older children is exophthalmic goitre or hyperthyroidism. This disease, although relatively frequent above ten years of age, is rare under five and very rare under three. The age of this two and one half year old, then, is very much against a diagnosis of hyperthyroidism. The absence of excessive perspiration, tremors, weakness, and nervousness is also at variance with this diagnosis.

Physical examination revealed a well nourished and well developed child, hardly in favor of hyperthyroidism. It would be interesting to know the exact weight. The temperature of 101 degrees can be explained by the pharyngitis, some other infectious process, or by a metabolic disorder. Rather important signs, I believe, are the extreme irritability and the elevated pulse rate, although pulse rates are so often variable in children. The respiratory rate is not striking. A blood pressure determination might have been helpful. There was a moderate exophthalmus and a narrowing of the palpebral fissures in this oriental child. It should be kept in mind that the exophthalmus of exophthalmic goitre is far more prominent in adults than in children. The above symptoms suggest a toxic goitre and

the mass felt in the neck was thought to be thyroid. We are not told whether this mass was soft, firm, or stony-hard, smooth, irregular, or nodular, tender or not tender, warm or "cold." There was no mention of a "bruit" which is frequently found in hyperthyroidism.

We may consider some of the other diseases of the thyroid at this moment. Carcinoma does not seem likely. This is usually a protracted disease, the gland is indurated and nodular, the adjacent lymph nodes are enlarged, and metastases to the lungs and bones are seen by x-ray. Acute thyroiditis is more plausible. However, the temperature should be higher and the gland warm, tense, and tender. The leucocytosis in this case favors acute thyroiditis but the signs and symptoms of thyrotoxicosis are against it and for hyperthyroidism. A simple goitre is unlikely unless the thyroid is not concerned in the primary pathology.

Other masses in the neck which are not thought to be involved in this child's illness but could conceivably be present as incidental findings to the primary disease are as follows: thyroglossal duct cyst, branchial cleft cyst, dermoid cyst, hygroma, fibroma, hemangioma, endothelioma, enlarged submaxillary gland or lymph node, and cellulitis.

Whether to tie the mass in the neck to that seen by x-ray in the supracardiac area is a question. I do not believe they are directly connected but can be indirectly associated.

This supracardiac shadow is thought to be a thymus or a widened superior vena cava. However, let us consider some of the things that must cause supracardiac shadows and try to rule them out:

1. Inflammatory reactions of the mediastinum with or without abscess formation. The characteristic findings of mediastinitis (high fever, dysphagia, cyanosis, and toxicity) do not fit in well with our case.

2. Mediastinal neoplasms: a. Lymphomas (lymphosarcoma, leukemia, and Hodgkins' disease) produce nodal enlargements which are rather typical by x-ray.

b. Neuromas are usually found in the posterior mediastinum as homogenous, sharply circumscribed shadows.

c. Cystic hygromas are usually associated with similar tumors in the neck. X-ray is not diagnostic.

d. Mediastinal cysts appear as asymmetrical sharply circumscribed shadows usually in the anterior mediastinum. Teeth and skeletal elements are visible in many of them.

3. Paraspinal abscesses, usually tuberculous in origin, produce bilateral widening of the mediastinal shadow. This widening is characteristically fusiform and symmetrical. Destructive changes may be seen in the vertebrae.

4. Thymus: This is the most common supracardiac shadow, particularly

in infants and young children. It is best seen roentgenologically on expiration and may appear globular, oval, columnar, or triangular. A very characteristic finding is the notched defect at the junction of the lower pole of the lobe of the thymus with the cardiac shadow. The thymus has long been thought to be interrelated to the endocrine glands and to have an endocrine function. Thymectomy in animals results in genital hypoplasia, enlargement of the adrenal cortex, compensatory hypertrophy of the thyroid, and retardation of growth in successive generations. Very important in this discussion, I believe, is the fact that the *thymus is frequently enlarged with hyperthyroidism*. We have an enlargement in the neck here, presumably thyroid, and a supracardiac mass, presumably thymus. Tumors of the thymus are rare. The most frequent cause of enlargement is simple hyperplasia of the gland. Very rare is edema, hemorrhage, and inflammation.

The laboratory findings of significance in this case are acetonuria, leucocytosis, and a hypoglycemia. Acetonuria occurs in infants and young children with febrile disorders, metabolic disease, digestive disturbances (particularly vomiting) and diabetes mellitus. The white cell count is twice normal with an increase in the polymorphonuclears. This suggests an infectious process such as thyroiditis rather than hyperthyroidism which is usually associated with a lymphocytosis. A little confusing is the low blood sugar, particularly if we are trying to make a diagnosis of hyperthyroidism. As we know, it is usually low in *hypo*thyroidism and elevated in *hyper*thyroidism. However, there are probably other factors in this case. A degree of starvation, for instance, could explain the acetonuria and the hypoglycemia.

The child went downhill rapidly and became stuporous 12 hours after admission with a rapid rise in temperature. The extremities were then flaccid and the reflexes absent. A spinal tap was negative. The child died 22 hours after being hospitalized.

This rapid course would seem to rule out many things such as tumors of the thyroid or thymus, Schüller-Christian disease, etc.

Taking everything into account, it would seem that hyperthyroidism with overwhelming toxicity and simple hyperplasia of the thymus would be the most likely diagnosis.

PATHOLOGICAL DISCUSSION

E. Clarence Rice, M.D.: The diagnosis is thyrotoxicosis, stage of crisis, due to a hyperplastic goiter.

The body was that of a well developed and nourished girl, having the appearance of a member of the yellow race, her estimated age being two and one half years. The thyroid was enlarged and red, weighing 26 gm., each lobe measuring 4.5 x 2.0 cm., the isthmus measured 1.0 x 0.5 cm.

The thymus was likewise larger than normal weighing 64 gm. and measuring 7.5 x 9.5 x 2.5 cm., being about the size of a male fist. The thoracic lymph nodes were not enlarged, but the mesenteric were. The heart was dilated and weighed 100 gm., measuring 8.5 x 7.0 cm., extending 4.0 cm. to the right of the midline. The musculature was of good tone. The lungs were normal. The abdominal viscera were somewhat heavier than normal and congested. Other than this they showed nothing remarkable, congestion being most noticeable in the liver and kidneys. The brain and pituitary appeared normal.

Microscopic examination revealed a reduction in the eosinophilic cells of the pituitary. The thyroid gland evidenced marked hyperplasia of the gland with papillary projections of the lining epithelium which was of columnar type. The gland acini were almost devoid of colloid, that remaining taking a light pink stain. The ovaries were the sites of a number of follicular cysts.

The pathologic diagnosis was:

1. Hyperplastic thyroid gland.
2. Hyperplasia of the thymus.
3. Dilatation of the heart.
4. Congestion and toxic degeneration of the liver.
5. Congestion of the liver and kidneys.
6. Follicular cysts of the ovaries.

Thyroid disease in the child is relatively uncommon and can be expected about one per cent as frequently as in the adult. Hyperthyroidism in a child of this age is quite rare and although the clinical picture, gross and microscopic findings are those of a hyperplastic goiter the patient evidently did not manifest any very noticeable signs of toxicity until a short time before death. The finding of an enlarged thymus is an expected finding in children with this type of thyroid dysfunction as was the dilated heart and toxic changes in the liver.

This is the first death to my knowledge of a patient in a thyroid crisis at this hospital.

Although thyrotoxicosis is a rather rare condition in children, it is interesting and to be expected that a much greater proportion of these patients have carcinomas than do adults.

NOTES

The Research Foundation of the Children's Hospital in collaboration with the Child Welfare Department is in the process of evaluating the effects of glutamic acid in patients showing mental retardation. In addition to the clinical and psychological evaluation done in the Child Welfare

clinic, a biochemical laboratory has been set up to determine if possible the metabolism of glutamic acid in the same group of patients. This study is just under way but a preliminary report is contemplated some time in 1949.

George William Ware, M.D. (*Burns*, p. 31) b. April 26, 1920, Clinton, Mass.; Holy Cross College; M.D. Georgetown Medical School, 1945; 9 mos. interneship Providence Hospital, Washington, D. C.; 6 months Resident in Pathology Georgetown University Hospital; 6 months Resident in Surgery Georgetown University Hospital, 9 mos. Children's Hospital, 6 mos. Georgetown University Hospital. "Regional Enteritis", J. of Ped.; "Roseola Infantum", J. of Ped.; "Intussusception" and "Patent Ductus Arteriosus"—to be published. Dr. Ware plans to specialize in Pediatric Surgery.

Claude A. Frazier, M.D. (*Clinico-Pathological Conference*) b. April 15, 1920, Knoxville, Tennessee. B.S. Chemistry, West Virginia Institute of Technology; M.D. Medical College of Virginia; interneship Medical College of Virginia; Assistant Resident in Pediatrics, Harriet Lane Home of the Johns Hopkins Hospital; 14 mos. Resident in Pediatrics, The Children's Hospital, Washington, D. C. "Pyloric Stenosis", "Prolapsus Uteri with Inversion in an Infant", "Empyema in Infants and Children (A Review of Cases)", "Sickle Cell Anemia Crisis in a One Month Old Infant", "Achondroplasia and Osteogenesis Imperfecta in an Infant". Dr. Frazier's plans for the future include a Residency in Allergy following which he hopes to teach Pediatrics.

Erratum

Dr. Perret's christian name was erroneously listed as James in the index section of the November issue. Dr. Perret's correct full name is Joseph Maxime Perret.